

REMARKS

By an Office Action dated December 17, 2003 in the file of the above-identified patent application the Examiner in charge of the application continued to reject the application on reasons under both §112 and §103. By this Response the applicants are responding to those grounds of rejection. Based on this response, and the accompanying RCE submitted herewith, reconsideration of the merits of this patent application is respectfully requested.

The Examiner first rejected Claims 1-12 and 17 under 35 U.S.C. §112, first paragraph, on the grounds that the application is not enabling for the claims as limited. In the Office Action, the Examiner said that the arguments did not address the problems of route of delivery of the vector to the analog. The claims above have been amended to specifically recite the route of delivery, which is the route of delivery which has been demonstrated to be effective in the examples presented in this patent application. The examples illustrate the delivery of the DNA into the vein of the test animal. Accordingly, it is believed that this ground of rejection is now obviate by the amendment to the claims made above and that the rejection under 35 U.S.C. §112, first paragraph, is now overcome.

Secondly, the Examiner continues to reject the application under 35 U.S.C. §103 as being unpatentable over Twisk et al. taken in view of several subsidiary references. In essence, the Examiner still continues to assert that the references teach that the truncated LDL receptor will interact with apoAB, and that the combination claimed by the applicants is obvious. The applicants continue to disagree with this assertion.

First, the Examiner has made a point of citing prior art which teaches that techniques of genetic engineering applied to mammals are not always effective in the way originally intended. Note that the examples of the present application recite specifically that the genetic construct, when delivered into the vein of an experimental animal, resulted in the lowering of serum cholesterol in that animal. The method claimed here actually works.

It is submitted herewith that the combination of elements recited by the present claims, which require a truncated LDL receptor, a localization domain to direct the truncated receptor to the endoplasmic reticulum, and the binding of the localized receptor to lipids in a manner that actually resulted in a lowering of serum cholesterol, was a result that was not fairly predictable from the prior art. The Examiner has constructed a rejection from comments and theories in the prior art. However, at most this prior art would teach one of ordinary skill in the art that what the applicants here have done was a worthy expedient to try to lower serum cholesterol. It was not clear, or even likely, from the teachings of this art, that

the applicants' method would work. It is submitted by the applicants that this rejection is a variant of an "obvious to try" rejection. The cited prior art does not make it clear that the claimed process would actually work to lower serum cholesterol. Note that the LDL receptor mediates both apoB secretion and reabsorption, and it was not clear that the localization recited by the applicants here would achieve the desired results, until the results presented here were achieved. The processing and secretion of cholesterol is a notoriously complex area, and there was not a reasonable expectation, prior to the work of the applicants here, that the lowering of serum cholesterol would actually be achieved.

In essence, it is submitted by the applicants that the combination of the uncertainty arising in general with techniques of genetic engineering, and the uncertainty inherent in dealing with a complex biological system such as cholesterol secretion, makes it unpredictable that the method described by the applicants here would actually work. That is, until the work of the applicants here described in the examples which demonstrates in experimental animals that the technique actually does work. Accordingly, the prior art lacked a reasonable expectation of success, and the method and vector of the present invention must be considered unobvious over this cited prior art. Accordingly, it is requested that this rejection be reconsidered and withdrawn.

A request for continued examination is submitted herewith so that this response will be fully considered by the Examiner.

Respectfully submitted,



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